REMARKS

The Advisory Action of March 9, 2005 addresses claims 1-3 and 5. The present paper amends claims 1 and 5 and adds new claims 6-8 for examination.

New claims 6-8 merely recite the features of claims 2 and 3 as dependent from claim 5. The amendments to claims 1 and 5 are supported by the specification at, e.g. page 2, last line (one or more SNP sites), and at page 19, lines 3-4 (98% detection). Claims 1 and 5 are also amended to clarify that the sample being assayed (the "plurality of nucleotide sequences") includes among those nucleotide sequences at least two SNP sites. Applicants wish to clarify that any one nucleotide sequence being amplified, though it may contain a plurality of SNP sites, may alternatively contain only one, or perhaps no, SNP site.

Rejection over Wang et al.

The Examiner maintains the rejection of claim 5 under 35 USC § 102(b) over Wang, asserting that Applicants argument about the number of SNP sites detected in the assay described by Wang overlooks the assay which included 558 loci. Applicants concede such is the case, but on close reading also note that in the assay for typing that many loci, only 50% of the sites present are detected. See, col. 3 on page 1080. However, the present claims recite that at least 98% of sites are detected, and thus the present invention as described in claim 5 is not anticipated by Wang and the instant rejection should be withdrawn.

Rejection over Walberger

The Examiner also maintains the rejection of claims 1 and 2 under 35 USC § 102(b) over Walberger. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

The Examiner first indicates that the instant rejection is maintained in part because of an apparent disagreement in claim interpretation. In particular, the Examiner suggests that the

present claims encompass typing of a single polynucleotide polymorphism site in the assay. The claims are presently amended to clarify that at least two SNP sites are typed in the claimed assay.

The Examiner also appears to interpret the claims as to require that the nucleic acid fragment subjected to typing must contain 100 SNP sites. This is not correct. As the Examiner has stated elsewhere in the Advisory Action, the claimed method requires that at least [two] sites be typed, and that the amount of DNA used in the assay is in the proportion of 10-40 ng per 100 sites.

Even with this broader interpretation of the claims, Walberger fails to anticipate the present invention. The Examiner takes a position that Walberger uses only 9 ng of DNA to for detection by a Light Cycler method, pointing out disclosure at page 72, first column.

The Examiner is incorrect that an amount of 9 ng of genomic DNA template is used for multiplex PCR. At page 71, second column. It is true that 9 ng of genomic DNA template was used in reactions for analysis in the "light cycler" format (see page 71, bottom of second column). This is further described at page 72, at the bottom of the second column, as being a "single probe" assay. On the other hand, it is stated that 100 ng of genomic DNA is used for an amplification with "wild type and mutant allele probes both ...". Therefore, Walberger insists that much more template DNA must be used for typing of a plurality of SNP sites. This is even explicitly stated by Walberger at page 77 at the top of the first column, "It should be noted that reactions in the ABI Prism 7700 require more reagents and time,... PCR is performed in a minimum volume of 50 µl ...". Applicants thus note the concentration of DNA of at least 1 ng/µl as described in the single probe assay (9 ng of genomic DNA per 9 µl reaction volume); at least 50 ng of DNA is therefore used by Walberger for typing of a plurality of SNPs in an assay.

Accordingly, Walberger does not anticipate the presently claimed invention and the rejection of claim 5 under 35 USC § 102(b) over Walberger should be withdrawn.

Rejection over Wang in view of Brookes

Claims 2 and 3 remain rejected under 35 USC § 103(a) as being unpatentable over Wang et al. in view of Brookes. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

The Examiner asserts that all of Applicants' arguments are directed to the Wang reference. This is not entirely correct. Applicants clearly argued that at least one feature of claims 2 and 3 that distinguished the invention over the combination of the references was the amount of DNA used in the assay, and that as neither of the references disclosed or suggested this amount of DNA, the combined references failed to establish *prima facie* obviousness of the invention.

The Examiner has clarified his position, pointing out that Wang does assert one assay, of 558 loci, that utilizes a proportion of DNA in the assay as recited in the present claims. Applicants have also amended the claims to indicate that at least 98% of the SNP sites that are present in the DNA being typed are detected. This feature of the invention is neither disclosed nor suggested by the combination of Wang with Brookes. That is, the combined references fail to suggest that 98% of the SNP sites in the sample being typed can be detected in an assay using from 10 to 40 ng of DNA per 100 sites to be assessed. Accordingly, claims 2 and 3 are unobvious in view of Wang and Brookes and the instant rejection should be withdrawn.

Alternatively, the result that at least 98% of SNP sites are detected using such a low amount of sample DNA may be viewed as a result that is unexpected by one of ordinary skill in the art who reads the references. That is, when the low level of 10-40 ng per SNP site assessed of sample DNA is used by Wang, only 50% of SNP sites present in the sample are detected. (This result may in fact be considered as teaching away from the present invention.) On the other hand, at least 98% of SNP sites are detected in the presently claimed method, an improvement that evidences unobviousness of the present method over Wang in view of Brookes.

The rejection of claim 3 under 35 USC § 103(a) over Wang in view of Walberger is also maintained. The Examiner submits that all of Applicants' prior arguments were directed to the amount of DNA used in the assay, which amount is asserted to be in fact recited in the Wang and Walberger references.

Applicants have pointed out above that the combination of the low amount of DNA used in the assay with the high rate of detection of SNP sites is a feature of the invention not disclosed or suggested by Wang. Indeed, as explained above, Wang shows that use of a proportion of DNA to SNP sites as recited in the present claims results in a low detection rate of about 50%. Thus, Wang in fact teaches away from the present invention. The combination of low sample input with high detection rate is also neither disclosed nor suggested by Walberger; and therefore the combination of these two references fails to disclose or suggest this feature of the invention. Accordingly, Wang taken with Walberger fails to establish *prima facie* obviousness of the claimed invention and the instant rejection should be withdrawn.

Applicants submit that, for the reasons given above, the present rejections should also not be applied against new claims 6-8.

The present application well-describes and claims patentable subject matter. The favorable action of allowance of the pending claims and passage of the application to issue is respectfully requested.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Mark J. Nuell (Reg. No. 36,623) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

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Respectfully submitted,

By _____

Mark J. Nuell, Ph.D.
Registration No.: 36,623
BIRCH, STEWART, KOLASCH & BIRCH, LLP
8110 Gatehouse Rd
Suite 100 East
P.O. Box 747
Falls Church, Virginia 22040-0747
(703) 205-8000
Attorney for Applicant